

**Remarks**

After entry of this amendment, claims 1-18, 20, and 23 will be pending. Claim 21 was cancelled in the preliminary amendment. Claims 18, 19, and 22 were cancelled in the response dated 12 March '04.

In response to a restriction and election of species requirement, the applicants originally elected to proceed with prosecution of the original restriction Group I and elected the species of example 2.

In the Office Action of 3/5/03, claims 18, 19, and 21 were withdrawn (the examiner failed to notice that claim 21 had been cancelled previously, and presumably meant to withdraw claims 18, 19, and 22), and claims 1-17 were rejected as anticipated by the disclosures of WO 98/27061, U.S. Patent 6,248,739 of Turner, and U.S. Patent 6,291,503 of Schoop.

In their response, applicants stated that they had reviewed the cited references, but did not find that the elected species was disclosed therein, and asked the examiner to identify where in the cited references the elected species was disclosed. Applicants also confirmed the withdrawal of claims 18, 19, and 22.

In the Official Action of 11/18/03, the examiner stated that each compound within the claims is a patentably distinct invention, each requires a separate search, there are far too many species to search, so the examination is limited to the elected species. The examiner made the restriction requirement final, and confirmed withdrawal of claims 18, 19, and 22. The examiner did not address the applicants' rebuttal of the original anticipation rejection.

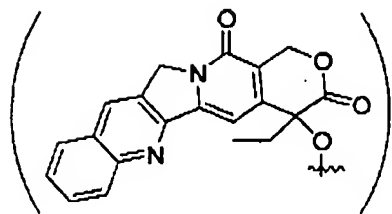
In their response of 12 March '04, the applicants cancelled withdrawn claims 18, 19, and 22, and requested withdrawal of the finality of the restriction requirement as well as the examiner's implied maintenance of the anticipation rejection.

In the advisory action, the examiner again ignored the applicants' argument that the anticipation rejection was defective and stated "...after an analysis of the prior art and the claims themselves it is clearly evident that the claims encompass so many compounds that to examine the next species and the next species and the next which will go on for a very long time is simply too time consuming, time that the patent office does not have to examine the breadth of these claims."

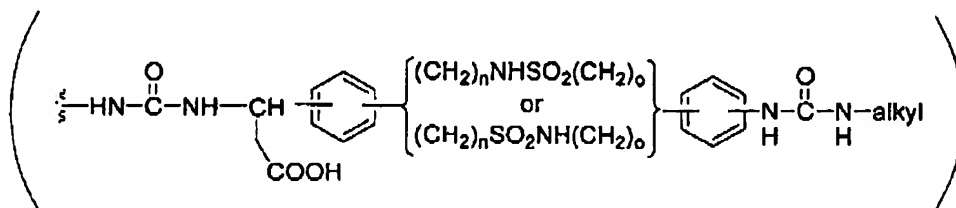
The examiner has not followed MPEP 803.02 in dealing with this application, but has instead simply rejected the elected species as anticipated in view of references which do not in fact disclose it, and has closed the prosecution.

If the examiner has determined that he is unable or unwilling to deal with this application, he is requested to have it reassigned to another examiner who can handle this continuing prosecution.

The applicants recognize that broad Markush claims are difficult to examine, and that MPEP 803.02 is not particularly practical or helpful. Nevertheless, it is necessary to deal with this application somehow in a reasonable practical way. In an attempt to facilitate further prosecution of the application, the applicants are now adding new claim 23. This claim is derived from claim 1 by selecting definitions of the various claim elements, which result in a recital of a small subset of similar compounds within the originally claimed larger group of conjugates. This subset includes most (but not all) of the exemplary compounds, including the previously-elected species, example 2. It is easy to search such a claim. One only needs to perform a substructure search for the camptothecin portion of the conjugate shown at the top of the structure in example 2



then perform another substructure search for the partial structure at the bottom of the formulae of the exemplary structures now covered by new claim 23



possibly perform a third substructure search for sequences of 5-8 naturally occurring amino acids, and finally, combine the results of these searches using the Boolean "and" operator to identify references which disclose compounds which include each of the searched-for subunits.

The same process can be employed to search for other subsets of conjugates which may be defined by further amendments during later prosecution of the application. Applicants will be happy to discuss reasonable restriction requirements with the examiner as prosecution proceeds.

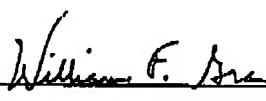
Respectfully submitted,

Reg. No.: 31018

Phone: (203) 812-2712

Date: 15 Sept 2004

West Haven, CT 06516-4175

  
William F. Gray

Bayer Pharmaceuticals Corporation

400 Morgan Lane